Original Article

Comparing the effect of intravenous dexamethasone, intravenous ondansetron, and their combination on nausea and vomiting in cesarean section with spinal anesthesia

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Abstract

Background: Nausea and vomiting are frequently seen in patients undergoing cesarean section (CS) under regional anesthesia. We aimed to compare the antiemetic efficacy of ondansetron and dexamethasone combination with that of the use of each agent alone to decrease the incidence of postdelivery intra- and post-operative nausea and vomiting during CS under spinal anesthesia.

Materials and Methods: A randomized, prospective, double-blind study was performed on 90 patients undergoing planned CS under spinal anesthesia. The patients received 4 mg ondansetron in Group O, 8 mg dexamethasone in Group D, and 4 mg ondansetron +8 mg dexamethasone in Group OD intravenously within 1–2 min after the umbilical cord was clamped. Frequency of postdelivery intra- and post-operative nausea and vomiting episodes was recorded.

Results: A total of 90 eligible patients were included in the study. There were 30 patients in Group O, 30 patients in Group D, and 30 patients in Group OD. Intraoperative nausea in Group D was more than the other two groups. Postoperative nausea in group OD was lesser than the other two groups. Intraoperative vomiting in Group OD was lesser than the other two groups. There was no statistically significant difference among the groups in postoperative vomiting ($P > 0.05$).

Conclusion: Combined use of dexamethasone and ondansetron for the same indication seems to increase the antiemetic efficacy.

Key Words: 5-hydroxytryptamine 3 antagonists, dexamethasone, intraoperative, nausea and vomiting, ondansetron, postoperative

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INTRODUCTION

Nausea and vomiting are seen in more than 80% of patients who have experienced cesarean section (CS) with spinal anesthesia.[1-3] Many factors affect this complication such as patient mental status, the kind of surgery, stretch of visceral

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peritoneum, decompensated hypotension, using narcotics, and factors which tighten the uterus.[4-6] In patients, this complication makes perilous problems, by preventing nausea and vomiting, they feel consent and comfort.[7] Although in most cases nausea and vomiting are controlled spontaneously, sometimes it can result in complications such as aspiration, suture dehiscence, esophageal rupture, subcutaneous emphysema, and pneumothorax.[8] Nausea and vomiting resulted in different problems such as delayed discharging from postanesthesia care unit, high length of hospital stay, high risk of aspiration, and serious problems. Ability to recognize which patient is in the high risk for nausea and vomiting and to do preventive acts, can yield in patient consent in postanesthesia care unit because most of them believe that nausea and vomiting are the results of postoperative pain.[9] Drugs for preventing this complication are given after clamping the umbilical cord of fetus.[10-12]

Ondansetron is a selective antagonist for receptor 5-hydroxytryptamine 3 and is very effective in the prevention and treatment of nausea and vomiting resulted from chemotherapy, intra- and post-operation. This medicine decreases nausea and vomiting of cesarean but it cannot control it completely.[13-15] Dexamethasone is reported to be a powerful antiemetic and anti-inflammatory medicine which can control nausea and vomiting completely.[16-19] The mechanism of antiemetic effect of dexamethasone is not completely known, but it is presumed that its effect occurs via inhibition of prostaglandin and producing anti-inflammatory feature and decreasing the amount of internal opioids.[18-20] Effective amount for being used as an antiemetic medicine is daily about 2.5 to 10 mg.[21,22] Being different mechanisms of nausea and vomiting, using combination of different medicine can be useful.[23]

De Oliveira *et al*. found out that in patient experiencing CS with epidural anesthesia who received 4 mg intravenous ondansetron in a prophylaxis manner, vomiting and their comportment were significant.[24] Jabalameli *et al*. concluded that nausea and vomiting and the comfort of patients experienced CS with spinal anesthesia who received intravenous ondansetron and midazolam, are very significant.[25]

This research aimed to compare the effects of ondansetron and dexamethasone alone and in combination on occurring nausea and vomiting in patients experienced CS with spinal anesthesia in Kosar Education and Treatment Center of Urmia University of Medical Sciences.

MATERIALS AND METHODS

In this prospective, randomized, double-blind study, sample size was calculated using Cochran's formula with confidence level and error level of 95% and 0.1, respectively. After obtaining verification and informed consent from Research Ethic Committee and understudied units, 96 female patients in Class 1 and 2 of American Statistical Association with the age range of 20–40 years who experienced cesarean with spinal anesthesia were selected. Patients with history of gastrointestinal disorders, motion disorders, drug hypersensitivity, glaucoma, preeclampsia, eclampsia, mental illness, and also patients, who took antiemetic medicines 24 h before section, were excluded from the research. There were 6 patients with these criteria and excluded [Figure 1].

Antiemetic medicines were provided in the form of syringes containing 5 ml of normal saline solution and were injected by a second party who was unaware of what the syringes contain.

Solutions were prepared as follows: For Group O (45 population), 4 ml ondansetron (Tehran Chemistry Co., Tehran, Iran) was added to 5 ml diluted normal saline, for Group D, the syringe contained 5 ml normal saline and 8 ml dexamethasone (Caspian Daru Co., Tehran, Iran), and for the last group (Group OD with 45 individuals) two syringes containing ondansetron and dexamethasone, as the same as the other two groups, were prepared and injected intravenously 1–2 min after cord clamping.

In the operating room, patients were monitored primarily by noninvasive blood pressure monitoring, electrocardiogram, and pulse oximetry. All patients received between 15 and 20 ml for each 1 kg (up to 1500 ml) normal saline before any treatment. Spinal anesthesia was injected via a 25-gauge needle, in a sitting position, and through a space between the third and fourth lumbar vertebrae, 12.5 mg hyperbaric marcaine was injected in subarachnoid space. Patients were placed in backward sleeping position and they were prevented from hypotension. Patient's bed was rotated to the left between 15° and 20° to prevent from aortocaval compression by the uterus. The patient received 2–3 L oxygen/min through a face mask. Every 1–3 min, patient's pressure was measured and it was used from 5 to 10 mg intravenous ephedrine or increasing the speed of infusion of normal saline to prevent from hypotension, if systolic blood pressure is below 100 mm Hg or more than 20% decrease in initial systolic blood pressure. Nausea and vomiting cases were

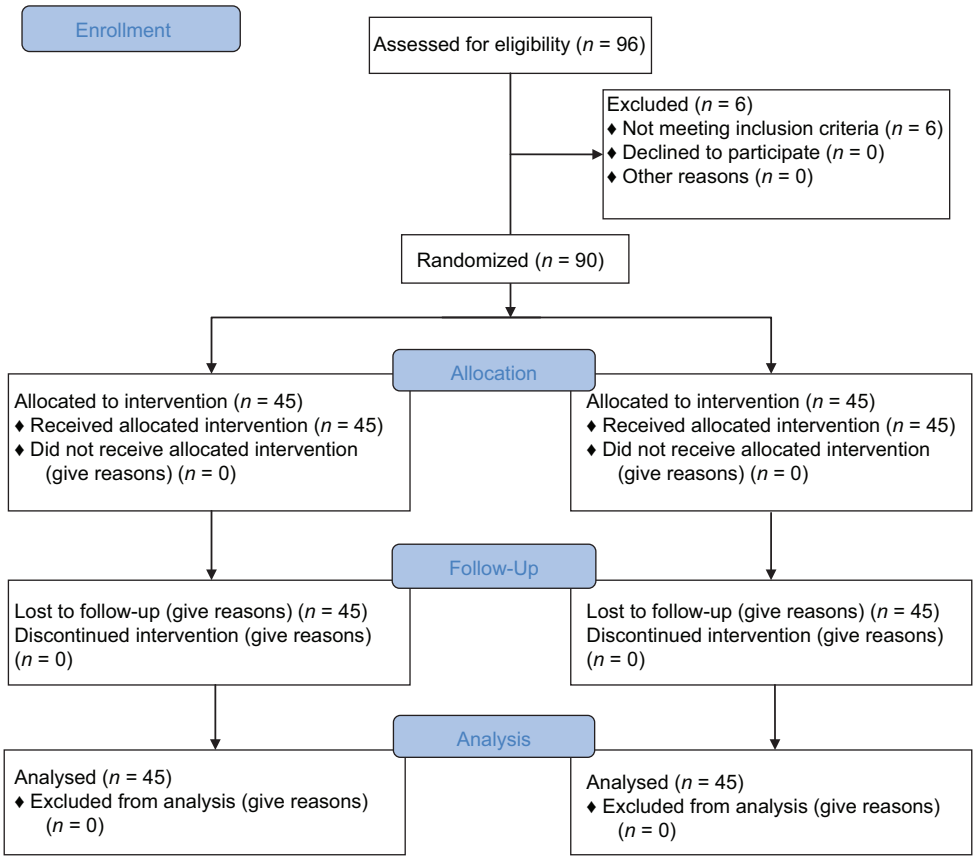

Figure 1: Study flowchart

analyzed and recorded for intra- and post-operation. Data were placed in prepared forms and were analyzed statistically.

The collected data were analyzed by SPSS for Windows, version 20.0 (SPSS, Chicago, IL, USA). In order to analyze the data, Fisher's exact test, Chi-square, and Fisher's exact test were used. In all comparisons, the significant level was considered <0.05.

RESULTS

The mean age of the women in dexamethasone group was 30.23 ± 5.78, in receivers of ondansetron was 30.36 ± 6.15, and in the third group, that is, with concurrent use of dexamethasone and ondansetron, was 31.40 ± 6.3. According to ANOVA test, there was no significant difference among these three groups in terms of age ($P = 0.71$).

The results of this study on reduction of nausea and vomiting in three treatment groups of dexamethasone, ondansetron, and combined dexamethasone and ondansetron, showed that "the complications such as "Intraoperative Vomiting" and "Vomiting in Recovery" among the three studied groups had no significant difference ($P > 0.05$), so that in each of the three groups, intraoperative and in recovery vomiting" were seen in more than 80% of patients, and there was no significant difference in the outcomes.

According to Fisher's exact test, there is a significant difference among the receivers of dexamethasone alone, ondansetron alone ($P = 0.03$), and the receivers of dexamethasone + ondansetron ($P = 0.00$). This difference can be also seen in the receivers of ondansetron alone and the receivers of dexamethasone + ondansetron ($P = 0.05$) regarding the numbers of the patients with complications.

However, complications such as "Intraoperative Nausea," "Nausea in Recovery," and "Shivering" were significantly different among the three groups ($P < 0.05$). According to the Fisher's exact test, there is not any significant difference among the receivers of dexamethasone alone, ondansetron alone ($P = 0.36$), and the receivers of dexamethasone + ondansetron ($P = 0.11$), but it can be seen a significant difference between the receivers of dexamethasone alone and the receivers of dexamethasone + ondansetron ($P = 0.02$), in respect of intraoperative vomiting.

According to the Fisher's exact test and Chi-square test, there is a significant difference between the receivers of dexamethasone with ondansetron (P = 0.04) and the receivers of dexamethasone with dexamethasone + ondansetron (P = 0.00), and also between the receivers of ondansetron and the receivers of dexamethasone + ondansetron (P = 0.02), in respect of having shivering after surgery.

In fact, ondansetron was more effective than dexamethasone and the combination of dexamethasone and ondansetron was more effective than the ondansetron. It has been shown that the combined dexamethasone and ondansetron completely removed the complications of caesarean with spinal anesthesia. It is also shown that the most occurred complications have been related to the shivering and the lowest complications were belonged to vomiting in recovery [Table 1 and Figure 2].

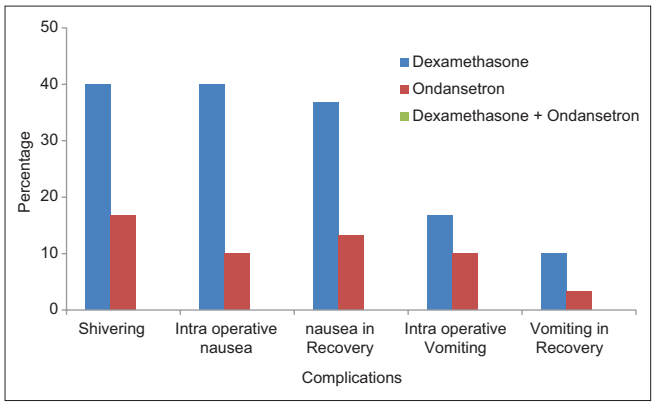

Figure 2: Bar chart percentage of cesarean section with spinal anesthesia complications in three treatment groups

DISCUSSION

In this randomized, double-blind, controlled trial, dexamethasone combined with ondansetron reduced the incidence of severe complications compared with ondansetron alone in patients undergoing CS with spinal anesthesia.

According to our results, nausea and vomiting after cesarean section occur in almost 20–30% of patients, which are the second common complaint made by them.[1] Different studies in this field showed that personal particulars of the patient and the way of anesthetizing are two important factors for this.[2] In patients, this complication makes perilous problems, by preventing nausea and vomiting, they feel consent and comfort.[3] Although in most cases nausea and vomiting are controlled spontaneously, sometimes it can result in complications such as aspiration, suture dehiscence, esophageal rupture, subcutaneous emphysema and pneumothorax in preventing this complication, and recognizing effective factors. This research showed that using dexamethasone + ondansetron is more effective than using dexamethasone alone and ondansetron alone and the results were statistically significant.

Pan and Moore compared the effect of intravenous ondansetron and metoclopramide and control group on prevention from nausea and vomiting, during the surgery and 24 h after that, in patients who experienced cesarean with epidural anesthesia. They found out that in patient experienced CS with epidural anesthesia who gained 4 mg intravenous ondansetron in a prophylaxis manner, existence of

Table 1: Comparison of the percentage of CS with spinal anesthesia complications in three groups

Complications	Groups			P^a	P^b	P^c	P^d
	D (%)	O (%)	OD (%)				
Intraoperative nausea							
Yes	12 (40)	3 (10)	0 (0)	<0.001	0.007	<0.001	0.076
No	18 (60)	27 (90)	30 (100)				
Nausea in recovery							
Yes	11 (36.7)	4 (13.3)	0 (0)	0.001	0.037	<0.001	0.038
No	19 (63.3)	26 (86.7)	30 (100)				
Intraoperative vomiting							
Yes	5 (16.7)	3 (10)	0 (0)	0.074	0.448	0.020	0.076
No	25 (83.3)	27 (90)	30 (100)				
Vomiting in recovery							
Yes	3 (10)	1 (3.3)	0 (0)	0.160	0.301	0.076	0.313
No	27 (90)	29 (96.7)	30 (100)				
Shivering							
Yes	12 (40)	5 (16.7)	0 (0)	<0.001	0.045	<0.001	0.020
No	18 (60)	25 (83.3)	30 (100)				

*Groups D shown dexamethasone, O shown ondansetron, OD shown ondansetron and dexamethasone. Level significant with Chi-square test shown with [a]Comparing tree groups, [b]Comparing groups D with O, [c]Comparing groups D with OD, and [d]Comparing O with OD, CS: Cesarean section

vomiting and comfort was significant compared to the patients who received metoclopramide and also to control group, while there was not any significant difference between them considering vomiting. The difference between this research and the study we have done is that we used spinal anesthesia. Nausea in patients who received ondansetron compared to patients who received dexamethasone, was lower during the surgery, but after the surgery, there was not any significant difference.[26,27]

Jabalameli *et al*. analyzed the effect of midazolam alone and ondansetron alone and also in combination with each other on nausea and vomiting of patients who experienced cesarean with spinal anesthesia. They concluded that nausea and vomiting in patients who received intravenous ondansetron + midazolam were more than the other two groups. In this research, it is used from dexamethasone instead of midazolam and reached the same results in respect of vomiting in recovery room.[28]

Browning *et al*., in a research, hypothesized that using 8 mg intravenous ondansetron decreases nausea and vomiting of patients who experienced cesarean with spinal and epidural anesthesia, compared to the control group. Variables such as shivering, nausea, itching, headache, and comfort of patients were measured intra- and post-operatively. There was not any significant difference between the two mentioned groups in respect of all these factors. Difference of our study is that we analyzed just patients who experienced cesarean with spinal anesthesia, and they used 8 mg ondansetron and compared it with the control group which affected the results significantly. In addition, shivering in patients who received ondansetron + dexamethasone was significantly low and it is remarkable.[29]

El-Deeb and Ahmady performed a research on three groups: (1) Using two-sided electrical stimulation in pericardium 6, half hour before spinal anesthesia, (2) using 4 mg intravenous ondansetron, half hour before spinal anesthesia, and (3) the controls. They measured and analyzed nausea and vomiting, intra and 24 h postoperation. They found out that nausea and vomiting in two first groups, during and 6 h after surgery, were lower than control group. In our study, nausea in patients who received ondansetron during after surgery was lower than in patients who received dexamethasone. We also analyzed the cases of vomiting, and found out that in receivers of dexamethasone, it was more than the other two groups. In recovery room, there was not any significant difference among three groups considering the existence of vomiting.[30]

Habib *et al*.[31] during a research for analyzing the effect of metoclopramide alone, in combination with ondansetron, adding to infusion of phenylephrine and comparing it with using infusion of phenylephrine alone in patients, who experienced elective cesarean with spinal anesthesia considering nausea and vomiting, concluded that using metoclopramide + ondansetron decreases nausea and vomiting compared to the other groups. The effect of ondansetron was also significant and decreases nausea and vomiting compared to patients who received dexamethasone. However, in recovery room there was not any significant difference between the two groups.

Demirhan *et al*. during a research on the effect of ondansetron + dexamethasone and each of them alone on nausea and vomiting in women who experienced cesarean intraoperative nausea and vomiting with spinal anesthesia, found out that there was not any significant difference among three groups which was contrary to our results. Nausea in dexamethasone group was more than the other groups, and then it was ondansetron group, and finally the group of ondansetron + dexamethasone. Considering intraoperative vomiting, dexamethasone group gained top place, but in the recovery room, there was not any significant difference among the groups. They did not analyze these two factors in the recovery room.[32]

CONCLUSION

Using a combination of ondansetron and dexamethasone in women who have experienced cesarean with spinal anesthesia can decrease intra- and post-operative nausea and vomiting, in the recovery room. It is also effective in decreasing the shivering in spinal anesthesia.

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Conflicts of interest
There are no conflicts of interest.

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